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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,717	01/08/2002	Yuki Wakabayashi	NITT.0052	8912

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/038,717	Wakabayashi
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 8, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-14* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *10/038,717*.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 3-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-10 are rejected over the repetition of the phrase, "to one or more solutions which contain different deoxynucleotides, respectively" in claims 3 and 4. It is not clear if more solutions and more different deoxynucleotides are claimed by the repetition of the same phrase twice or it is a typo. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Nyren (PCT International Publication Number WO 98/28440) (July 2, 1998).

Nyren teaches a method of analysis of DNA sequence, which comprises;

a) degrading, by apyrase, adenosine 5'-triphosphate contained in the reagent (Abstract and page 34, lines 2-4 and Claims 1-3 and Results Section);

b) conducting the extension reaction (Abstract, page 33, line 22 to page 34, line 27 Claims 1-3 and Results Section).

c) detecting the pyrophosphoric acid generated by the extension reaction (Abstract and page 33, line 22 to page 34, line 27 Claims 1-3 and Figure 1 and Results Section).

Nyren teaches a method, wherein the apyrase has been immobilized on a solid (Claim 4).

5. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Hyman (U.S. Patent 4,971,903) (November 20, 1990).

Hyman teaches a method of analysis of DNA sequence (Abstract), which comprises;

a) degrading, by pyrophosphatase, pyrophosphoric acid contained in a reagent (Abstract and Figure 1 and Column 3, lines 4-64);

b) conducting the extension reaction (Abstract, and Figure 1 and Example).

c) detecting the pyrophosphoric acid generated by the extension reaction (Abstract and Figures 1, and 5 and Claims 1-2 and Example).

Hyman teaches a method, wherein the pyrophosphatase has been immobilized on a solid (Figure 1 and Column 3, lines 4-47).

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 9-13 are rejected under 35 U.S.C. 103(a) over Hyman (U.S. Patent 4,971,903) (November 20, 1990) in view of Nyren (PCT International Publication Number WO 98/28440) (July 2, 1998).

Hyman teaches the method of analysis of DNA sequence of claims 1-8 as described above.

Hyman does not teach the method, wherein the base at the 3' terminus of the primer is complementary to the base one base behind the 3' terminus site of a single nucleotide polymorphism of the target nucleic acid, and wherein the second or third base from the 3' terminus of the DNA primer has been substituted with a base not complementary to the base sequence of the target nucleic acid.

Nyren teaches the method, wherein the base at the 3' terminus of the primer is complementary to the base one base behind the 3' terminus site of a single nucleotide

Hyman teaches a method of analysis of DNA sequence which comprises adding pyrophosphatase to one or more solutions which contain different deoxynucleotides, at least one of which is an analogue thereof, thereby degrading pyrophosphoric acid contained in the solutions (Figure 1 and Column 3, lines 4-64 and Column 5, first paragraph), and

extending a DNA primer, which has been hybridized to a target nucleic acid via a complementary strand, by using the DNA primer, DNA polymerase and at least one of the solutions obtained in the step and detecting pyrophosphoric acid thus generated by the extension reaction into adenosine 5'-triphosphate in the presence of adenosine 5'-phosphosulfate and ATP sulfurylase, and detecting luminescence caused by chemiluminescence reaction containing the adenosine 5'-triphosphate, a luminescence enzyme and a luminescence substrate (Figure 1 and Column 3, line 65 to Column 5, line 66 and Claims 1-7 and Column 7, line 15 to Column 10, line 61).

Hyman inherently teaches a method comprising a step of removing or inactivating the pyrophosphatase in each of the solutions (Figure 1 and Column 3, line 65 to Column 4, line 62).

Hyman teaches a method, wherein the first step comprises adding the pyrophosphate to at least one of the DNA-primer-containing solution (Figure 1 and Example).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

polymorphism of the target nucleic acid, and wherein the second or third base from the 3' terminus of the DNA primer has been substituted with a base not complementary to the base sequence of the target nucleic acid (Page 27, second paragraph to page 28, whole page).

Hyman does not teach the method, wherein deoxyadenosine 5'-alpha-thiotriphosphate is used for analysis of DNA sequence.

Nyren teaches the method, wherein deoxyadenosine 5'-alpha-thiotriphosphate is used for analysis of DNA sequence (Claim 9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the base at the 3' terminus of the primer is complementary to the base one base behind the 3' terminus site of a single nucleotide polymorphism of the target nucleic acid, and wherein the second or third base from the 3' terminus of the DNA primer has been substituted with a base not complementary to the base sequence of the target nucleic acid and wherein deoxyadenosine 5'-alpha-thiotriphosphate is used for analysis of DNA sequence of Nyren with the method of analysis of DNA sequence of Hyman since Nyren states, "The assay technique is very simple and rapid, thus making it easy to automate by using a robot apparatus where a large number of samples may be rapidly analyzed (Page 14, fourth paragraph, first sentence)". Nyren further provides motivation as Nyren states, "The difference in primer extension efficiency by the DNA polymerase of a matched over a mismatched 3'-terminal can then be used for single-base discrimination. Thus, the presence of the mutated DNA sequence can be distinguished over the non-mutated sequence (Page 28, lines 16-21)". An

ordinary practitioner would have been motivated to combine and substitute the method, wherein the base at the 3' terminus of the primer is complementary to the base one base behind the 3' terminus site of a single nucleotide polymorphism of the target nucleic acid, and wherein the second or third base from the 3' terminus of the DNA primer has been substituted with a base not complementary to the base sequence of the target nucleic acid and wherein deoxyadenosine 5'-alpha-thiotriphosphate is used for analysis of DNA sequence of Nyren with the method of analysis of DNA sequence of Hyman in order to achieve the express advantages of a system, as noted by Nyran, of an assay technique which is very simple and rapid, thus making it easy to automate by using a robot apparatus where a large number of samples may be rapidly analyzed and which further provides difference in primer extension efficiency by the DNA polymerase of a matched over a mismatched 3'-terminal which can be used for single-base discrimination.

Moreover, it is *prima facie* obvious that selection of the specific nucleotide modification of the primer at the 3' end represents routine optimization with regard to detection of specific single nucleotide polymorphism which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the the specific nucleotide modification of the primer at the 3' end was other than routine, that the

products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

8. Claim 14 is rejected under 35 U.S.C. 103(a) over Hyman (U.S. Patent 4,971,903) (November 20, 1990) in view of Nyren (PCT International Publication Number WO 98/28440) (July 2, 1998) further in view of Abramson et al. (U.S. Patent 5,795,762) (August 18, 1998).

Hyman in view of Nyren teach the method of claims 9-13 as described above.

Hyman in view of Nyren do not teach the method, wherein the extension reaction is conducted by degrading the strand, which has been extended by the extension reaction, from the 5' terminus thereof by the 5'...>3' exonuclease reaction and repeating complementary strand hybridization of the DNA primer to the target nucleic acid.

Abramson et al. teach the method, wherein the extension reaction is conducted by degrading the strand, which has been extended by the extension reaction, from the 5' terminus thereof by the 5'...>3' exonuclease reaction and repeating complementary strand hybridization of the DNA primer to the target nucleic acid (Column 2, lines 46-54 and Column 36, lines 37-51).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the extension reaction is conducted by degrading the strand, which has been extended by the extension reaction, from the 5' terminus thereof by the 5'...>3' exonuclease reaction and repeating complementary strand hybridization of the DNA primer to the target nucleic acid of Abramson et al in the method of

Hyman in view of Nyren since Abramson et al states, "However, an enhanced or greater amount of 5' to 3' exonuclease activity in a thermostable DNA polymerase may be desirable in such an enzyme which is used in a homogeneous assay system for the concurrent amplification and detection of a target nucleic acid sequence. (Column 2, lines 46-50)". Abramson et al. further provides motivation as Abramson et al states, "In addition to the homogeneous assay system described above, the thermostable DNA polymerases of the present invention with enhanced 5' to 3' exonuclease activity are also useful in other amplification systems, such as transcription amplification system, in which one of the PCR primers encodes a promoter that is used to make RNA copies of the target sequence. In similar fashion, the present invention can be used in a self-sustained sequence replication (3SR) system, in which a variety of enzymes are used to make RNA transcripts that are then used to make DNA copies, all at a single temperature. By incorporating a polymerase with 5' to 3' exonuclease activity into a ligase chain reaction (LCR) system, together with appropriate oligonucleotides, one can also employ the present invention to detect LCR products (Column 36, lines 37-51)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the extension reaction is conducted by degrading the strand, which has been extended by the extension reaction, from the 5' terminus thereof by the 5'...>3' exonuclease reaction and repeating complementary strand hybridization of the DNA primer to the target nucleic acid of Abramson et al in the method of Hyman in view of Nyren in order to achieve the express advantages of a system, as noted by Abramson et al, of an assay technique with an enhanced or greater amount of 5' to 3' exonuclease activity in a

thermostable DNA polymerase that may be desirable in such an enzyme which is used in a homogeneous assay system for the concurrent amplification and detection of a target nucleic acid sequence and which is also useful in other amplification systems, such as transcription amplification system, in which one of the PCR primers encodes a promoter that is used to make RNA copies of the target sequence and which also can be used in a self-sustained sequence replication (3SR) system, in which a variety of enzymes are used to make RNA transcripts that are then used to make DNA copies, all at a single temperature and which can also be employed to detect LCR products.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti , Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

February 26, 2003

Arun kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER